USDA Foreign Agricultural Service

GAIN Report

Global Agriculture Information Network

Template Version 2.09

Voluntary Report - public distribution

Date: 4/21/2004

GAIN Report Number: E24069

European Union

Biotechnology

Antibiotic Resistance Marker Genes

2004

Approved by:
Norval Francis
U.S. Mission to the European Union, Brussels

Prepared by:
Stan Cohen

Report Highlights:
The European Food Safety Authority's (EFSA) Scientific Panel on Genetically Modified Organisms (GMO) published on April 19 an opinion concerning the utilization of antibiotic resistance genes (ARGMs) as marker genes in genetically modified plants. In the opinion issued, EFSA categorizes the ARGMs into three groups: 1) no restrictions are required in their use for field experimentation or for placing on the market; 2) these ARMGs should be restricted to use in field trials; and 3) these ARMGs should not be present in GM plants placed on the market nor in plants used for experimental field trials.

Includes PSD Changes: No
Includes Trade Matrix: No
Unscheduled Report
Brussels USEU [BE2]
[E2]

The European Food Safety Authority's (EFSA) Scientific Panel on Genetic Modified Organisms (GMO) published on April 19 an opinion relating to the utilization of antibiotic resistance genes as marker genes in genetically modified plants. This evaluation has been carried out by the GMO Panel as a "self-tasking" exercise in order to provide guidance to applicants, Member States and the European Commission regarding the safe use of antibiotic resistance marker genes (ARMGs) in the selection of transgenic events in plants. The Panel has sought to address this question as a matter of urgency given concerns that the use of such marker genes could potentially lead to increased resistance to antibiotics in humans and animals as a result of gene transfer from genetically modified (GM) plants to bacteria.

The GMO Panel concluded that the frequency of gene transfer is very low for all ARMGs considered. In its opinion, the GMO Panel took into account the prevalence of antibiotic resistance among bacteria in the intestine or in the environment (soil, plant, water…) and the extent of use of the antibiotics in question as well as their clinical importance for human and animal therapy. Based on this evaluation, the Panel has categorized the ARMGs considered into three groups, and has identified best practices for the safe use of each group, taking into account their respective potential influence on human health and on the environment.

During the process of genetic modification of plants and other organisms, marker genes are normally used in order to facilitate the selection and identification of genetically modified cells containing the gene of interest among the vast majority of untransformed cells in the host organism. Marker genes with a resistance to specific antibiotics are often utilized for such purposes. A concern with respect to antibiotic resistance marker genes (ARMGs) is the theoretical possibility that the clinical therapy of orally administered antibiotics could be compromised through inactivation by antibiotic resistance proteins present in foods derived from GM plants containing an ARMG.

In light of the growing number of applications for placing on the market of GM plants and the potential impact of ARMGs on human health and on the environment, the European Food Safety Authority's (EFSA) Scientific Panel on Genetically Modified Organisms (GMO) proposed to undertake a risk assessment on the use of antibiotic resistance genes as marker genes in genetically modified plants. In evaluating the potential risks associated with specific ARMGs for humans or the environment, the Panel took into account the likelihood of horizontal gene transfer from GM plants to microbes and the potential impact of such gene transfer where naturally occurring resistance to the relevant antibiotics exists in the microbial gene pool. The Panel also considered the current usage of the antibiotics concerned in clinical and veterinary medicine.

Commenting on the Panel's conclusions, Dr. Harry Kuiper, Chair of the GMO Panel stated: "The Panel has confirmed that ARMGs are in the majority of cases still required in order to ensure the efficient selection of transgenic events in plants. From a risk assessment perspective it is important to note that gene transfer from GM plants to bacteria is considered to be a very unlikely event. In case of the rare event that gene transfer takes place, its potential impact on humans and the environment should be evaluated against the natural presence of antibiotic resistance genes in the environment and in bacteria present in the intestine. The importance of the specific antibiotic to human and animal therapy should also be considered."

In order to provide further guidance on the use of ARMGs, the Panel has classified those evaluated into 3 groups based on their biological distribution and taking into account the current importance of the antibiotics concerned to human and veterinary medicine. Such a

classification will help to foster best practices for the safe use of ARMGs in plant biotechnology.

Background

Directive 2001/18/EC (on the deliberate release into the environment of genetically modified organisms) requires that GMOs which contain genes expressing resistance to antibiotics utilized for medical or veterinary treatment are taken into particular consideration when carrying out an environmental risk assessment. The overall aim is to identify and phase out in GMOs those ARMGs which may have adverse effects on human health or on environmental safety.

The GMO Panel has proposed the following classification for ARMGs:

• Group 1 ARMGs contains antibiotic resistance genes which (a) are widely distributed among soil and enteric bacteria and (b) confer resistance to antibiotics which have no or only minor therapeutic relevance in human medicine and have only restricted use in defined areas of veterinary medicine. This refers to the antibiotic resistance genes nptII conferring resistance to the antibiotics kanamycin and neomycin with a 13-year history of safe use in food crops and the hph gene which encodes for a protein that inactivates hygromycin, an antibiotic that is not utilized in human clinical medicine. No restrictions are required with this class of marker genes either for field experimentation or for placing on the market.

• Group 2 ARMGs contains antibiotic resistance genes which (a) are widely distributed in micro-organisms in the environment and (b) confer resistance to antibiotics which are used for therapy in defined areas of human and veterinary medicine. This group includes genes which confer resistance to chloramphenicol (CmR gene), ampicillin (ampr gene) and streptomycin and spectinomycyn (aadA gene). The use of these genes should be restricted to field trial purposes and not be present in GM plants placed on the market.

• Group 3 ARMGs contains antibiotic resistance genes which confer resistance to antibiotics highly relevant for human therapy like the nptIII gene conferring resistance to amikacin and the tetA gene conferring resistance to tetracyclines. Irrespective of considerations about the realistic importance of the health threat, these genes should be avoided in the genome of transgenic plants to ensure the highest standard of preventive health care. Therefore these ARMGs should not be present in GM plants placed on the market or in plants used for experimental field trials.

The opinion is available on the EFSA web site at:
http://www.efsa.eu.int/science/gmo/gmo_opinions/384

Visit our website: our website www.useu.be/agri/usda.html provides a broad range of useful information on EU import rules and food laws and allows easy access to USEU reports, trade information and other practical information. E-mail: AgUSEUBrussels@usda.gov

Related reports from USEU Brussels:

Report Number	Title	Date Released
E24045	Safe as Conventional Rapeseed	03/04/04
E23231	The European Food Safety Authority	12/11/03

E23233	Safe as Conventional Corn	12/11/03
E23234	BT 11 Sweet Corn	12/12/03